Determination of NDMA Impurity in Ranitidine using the ACE C18-AR

ACE® Ultra-inert UHPLC & HPLC Columns

Application #AN7030

Ranitidine is a popular prescriptive drug used to decrease the amount of acid created by the stomach and it is included on the World Health Organisation's 'Model List of Essential Medicines'.

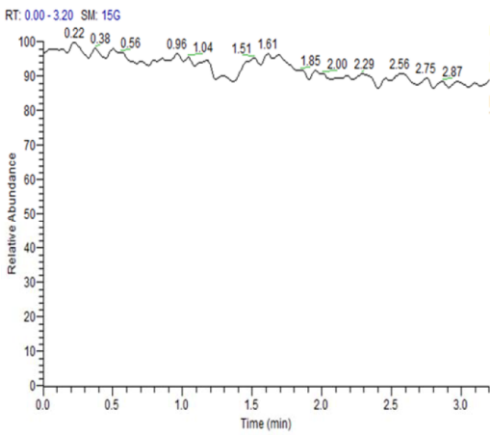
The U.S. Food and Drug Administration has announced that low-levels of the impurity N-nitroso-di-methylamine (NDMA) have been detected in some medicines containing ranitidine. NDMA is classified as a 'probable human carcinogen' based on results from laboratory tests. It is also a known environmental contaminant that can be found in water and foods such as dairy products, vegetables and meat.

The FDA have recently posted an LC-HRMS method using the ACE 3 C18-AR, 50 x 4.6 mm column (ACE-119-0546), which can be used by regulators and industry to detect nitrosamine impurities in ranitidine drug substances and drug products, with an LOQ level of 1.0 ng/mL. High sensitivity detection is achieved by monitoring the accurate *m/z* value of the protonated impurity ion.

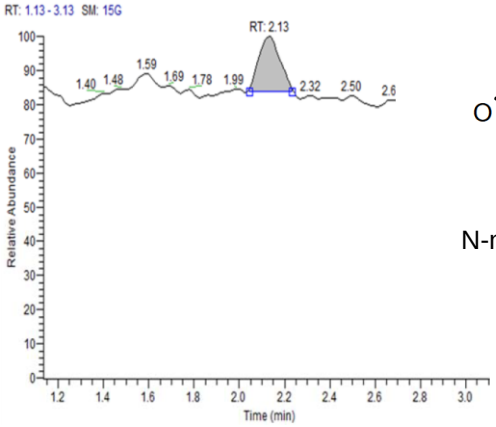
For further information regarding the method visit https://www.fda.gov/media/130801/download

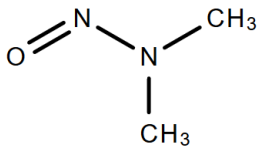
NDMA Impurity, Extracted Ion Chromatograms (EIC), *m/z* 75.0553

Methanol Blank



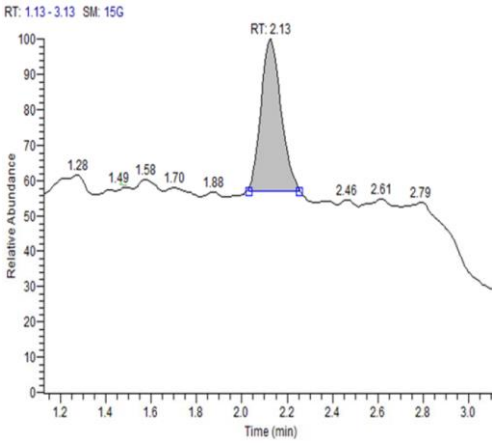
NDMA (2.0 ng/mL Standard)



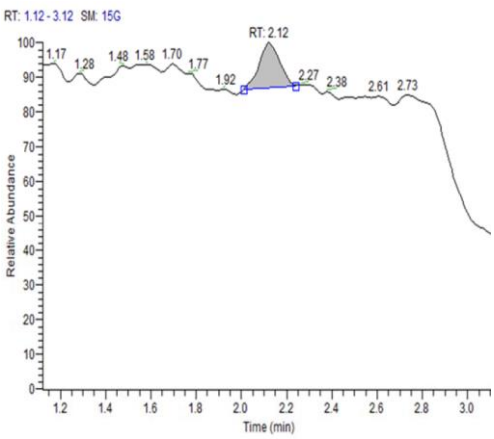


N-nitroso-di-methylamine (NDMA)

NDMA (Ranitidine Drug Substance)



NDMA (Ranitidine Drug Product)



Determination of NDMA Impurity in Ranitidine using the ACE C18-AR

ACE®
Ultra-inert
UHPLC & HPLC Columns

Application #AN7030

Conditions

Column:	ACE 3 C18-AR
Dimensions:	50 x 4.6 mm
Part Number:	ACE-119-0546
Mobile Phase:	A: 0.1% formic acid in water B: 0.1% formic acid in acetonitrile

Time (mins)	%B
0	5
1.0	5
3.0	20
7.0	100
9.0	100
9.1	5
14.0	5

Flow Rate:	0.5 mL/min
Injection:	3 µL
Column Temperature:	30 °C
Autosampler Temperature:	4 - 8 °C
Needle Wash:	80:20 methanol:water with 0.1% formic acid
Detection:	Thermo-Fisher Scientific Q Exactive Mass Spectrometer PRM, Positive Mode

Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS) Method for the Determination of NDMA in Ranitidine Drug Substance and Drug Product. *U.S. Food and Drug Administration*, FY19-177-DPA-S (Data copied 02 October 2019). https://www.fda.gov/media/130801/download